Original Article

Hepatitis C testing and infection rates in bipolar patients with and without comorbid substance use disorders

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Objectives: To determine and compare hepatitis C (HCV) screening and testing rates among four groups: those with (i) bipolar disorder [BD group (history of BD but no substance use disorder)]; (ii) substance use disorders [SUD group (history of SUD but no BD)]; (iii) co-occurring disorders [DD group (history of both BD and an SUD)]; and (iv) a control group (no history of either bipolar disorder or substance use disorder). Our hypothesis was that HCV antibody testing rates and HCV prevalence would be higher in the BD, SUD, and DD groups than the control group.

Methods: Data were retrospectively collected on 325,410 patients seen between 1998 and 2004 within facilities and clinics of the Veterans Integrated Service Network (VISN) 20 Northwest Veterans Health Care Administration from electronic medical records. HCV screening and prevalence rates were compared between the BD, SUD, DD, and control groups. Odds ratios and relative risks were determined and compared between groups.

Results: Patients in the BD, SUD, and DD groups had been tested at a higher rate than controls and were at increased risk for HCV infection compared with controls. These high-risk groups had a 1.31-fold, 4.86-fold, and 5.46-fold increase in the relative risk of HCV infection, respectively. Overall, compared to the control group, the relative risk of a patient having HCV if he or she had BD (with or without an SUD) was 3.6.

Conclusions: Patients with BD and comorbid SUD had an over fourfold increase in relative risk for HCV than our control group and a similar risk as patients in our SUD group. Furthermore, even if bipolar patients did not have a comorbid SUD (the BD group), their relative risk of HCV was significantly higher than that of the control group. This suggests that patients with BD, particularly those with a comorbid SUD, should be screened and tested for HCV.

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Epidemiologic studies show that, among Axis I diagnoses, bipolar disorder (BD) has been associated with the highest risk for substance use disorder (SUD) comorbidity (1, 2). Studies suggest that over 50% of bipolar patients have a lifetime SUD comorbidity and that this comorbidity confers a higher risk of suicide attempts, hospitalizations, more mood episodes and more days ill (3, 4). Although studies suggest that the percentage of bipolar patients with current SUDs is approximately 5% and therefore much less than the percentage of bipolar patients with lifetime substance use comorbidity (5, 6), both bipolar patients with a current or a past SUD had more lifetime suicide attempts and a significantly lower quality of life than bipolar patients without an SUD (7).

Chronic hepatitis C (HCV) is the most common blood-borne viral infection in the USA and approximately 1.8% of the general population is chronically infected (8) . Injection drug use (IVDU) currently represents the primary mode of transmission for HCV and it is estimated that approximately 60% of the 4 million cases of HCV and around 60%–70% of the 35,000 new cases of HCV in the USA each year are a direct result of IVDU behavior (9, 10). Various cross-sectional seroprevalence studies suggest that 60–90% of injection drug users are HCV antibody-positive (11). However, relative to the general population, the prevalence of HCV is also high among non-injection drug users. One study of 700 non-injection drug users (heroin, cocaine, or crack) showed that the prevalence of HCV ranged from 5% to 29%, depending on age, gender, study location, and drugs used (12).

While those with IVDU are clearly at greater risk for HCV, those with BD may also be at greater risk for both HCV and its related hepatic morbidity. Increased risk may come from some bipolar patients' participation in high-risk behaviors like intermittent/episodic drug use or hypersexuality when manic. In addition, alcohol use disorders are relatively common in bipolar patients, which may increase the likelihood of high-risk behaviors as well as increase risk of progression of liver disease secondary to alcohol use in those patients with HCV. Screening, testing, and appropriately treating HCV in the bipolar population may reduce the progression of liver disease and decrease liver-related side effects of medications used to treat BD.

The purpose of this study was to determine the prevalence of HCV in bipolar patients who received care in Veterans Integrated Service Network (VISN) 20 facilities and clinics of the US Veterans Health Care Network. We determined testing and infection rates among four groups of patients: (i) those with bipolar disorder [BD group (history of BD but no SUD)]; (ii) those with substance use disorders [SUD group (history of SUD but no BD)]; (iii) those with co-occurring disorders [DD group (history of both BD and an SUD)]; and (iv) a control group (no history of either BD or an SUD). We hypothesized that patients with BD, SUD and DD would be more likely to have been screened and tested for HCV and have higher infection rates than controls.

Methods

We collected data on 325,410 patients treated at any facility in the Northwest VISN 20 between January 1998 and December 2004. This includes eight medical centers and 17 community-based outpatient clinics distributed throughout Alaska, Washington, Oregon, and Idaho. Data were extracted from the VISN 20 Consumer Health Information and Performance Sets (CHIPS) Data Warehouse, which is a collection of databases extracted from the electronic patient medical records of each facility. Portland VA Medical Center Institutional Review Board approval was obtained for data collection and analysis.

We collected data on demographics, psychiatric diagnoses, HCV laboratory results, and clinic attendance. Laboratory results included tests performed between 1994 (the earliest date of data collection for the database) and 2004. We excluded non-veterans who did not receive regular care from the VA but had records in the electronic database.

HCV status

A patient was considered to have been tested for HCV if he or she had at least one HCV lab result in his or her record. Accepted lab results included: an HCV antibody test; an HCV viral load measured by polymerase chain reaction (PCR); an HCV recombinant immunoblot assay (RIBA); or an identifiable HCV genotype. Patients who were antibody-positive and either RIBA-positive or PCR-positive, or who had an identifiable HCV genotype were considered to have chronic hepatitis C (HCV-positive). Patients with negative antibody test results were considered to be HCV-negative for purposes of data analysis (not exposed to the hepatitis C virus or uninfected). False positives were those patients who had positive HCV antibody tests but were negative by RIBA confirmation and PCR-negative (no virus detectable). False positives were considered HCV-negative for purposes of data analysis.

Substance use disorders

A patient was considered to have an SUD if the patient's medical record included a DSM-IV-TR (Text Revision) code for substance abuse or dependence (with the exception of nicotine dependence).

Bipolar disorder

A patient was considered to have BD if the patient's medical record included a DSM-IV-TR code for either bipolar I, bipolar II, or bipolar not otherwise specified (NOS).

Based on the above definitions, we assigned patients to one of four possible groups: (i) BD group; (ii) SUD group; (iii) DD group, or (iv) control group.

We downloaded data from the VISN 20 Data Warehouse into a local database using structured query language (SQL) queries, where they were organized and exported to SPSS 11.0, SPSS Inc., Chicago, IL, US for analysis. Bivariate models were used to generate the odds ratios (ORs).

Results

Within the total sample (n = 325,410), patients were predominately male (93.3%), middle-aged (61.3 ± 15.8 years), and Caucasian (86.0%). The BD group had twice as many women (15.4%) as the comparison groups (Table 1). The following percentages of patients within the total sample met criteria for each risk group: (i) BD group: 1.5% (n = 5,026); (ii) SUD group: 11.7% (n = 37,970); (iii) DD group: 1.5% (n = 4,724); (iv) control group 85.3% (n = 277,690).

Within the total sample, 40% (n = 130,021) of patients had been tested for HCV. Relative to controls, those in the BD, SUD and DD groups were significantly more likely to have been tested. HCV testing had been administered to 59.8% (3,006/5,026) of the BD group, 69.1% (26,249/37,970) of the SUD group, 81.7% (3,860/4,724) of the DD group, and 34.9% (96,908/277,690) of the control group (Fig. 1). Patients in the BD group [OR = 2.78, 95% confidence interval (CI): 2.62–2.94; $p < 0.001$], SUD group (OR = 4.18, 95% CI: 4.08–4.28; $p < 0.001$) and DD group (OR = 8.33, 95% CI: 7.74–8.98; $p < 0.001$) had increased testing rates relative to patients in the control group.

Table 1. Demographic characteristics of study groups

Group	n (%)	Mean age (years)	Female (%)	Caucasian (%)
Total sample	325,410 (100.0)	61.3	6.7	86.0
BD only	5,026 (1.5)	55.6	15.4	90.9
SUD only	37,970 (11.7)	56.7	3.8	83.1
DD group	4,724 (1.5)	52.3	7.1	87.9
Controls	277,690 (85.3)	62.2	6.7	86.0

BD = bipolar disorder; SUD = substance use disorder; DD = co-occurring BD and SUD.

Of all patients tested for HCV within the total sample, 10.4% (n = 13,531) tested positive. The percentage of patients testing positive within each group were as follows: 7.1% (n = 214) of the BD group; 26.4% (n = 6,922) of the SUD group; 29.6% (n = 1,142) of the DD group, and 5.4% (n = 5,253) of the control group. Compared with the control group, the three diagnostic groups had a 1.31-fold, 4.86-fold, and 5.46-fold increase in the relative risk of HCV infection, respectively.

Of the total sample, 3% (9,750/325,410) were bipolar patients either with or without a history of substance abuse (BD and DD groups combined). Of these, 70.4% (6,866/9,750) had been tested for HCV, and of those tested, 19.7% (1,356/9,750) were HCV-positive. Overall, compared with the control group, the relative risk of a patient having HCV if he or she had BD was 3.60.

Discussion

In our study we found that 10.1% of veterans tested were HCV-positive. This is much higher than the US general population prevalence of 1.8% and also higher than that found in the 2005 VA prevalence study, which examined a national sample of 145 Veterans Affairs health care facilities and found an HCV prevalence of 5.4% among veterans using the VA Health Care Network (8, 13). The overall elevated risk in veterans as compared to the general population is likely due to a higher prevalence of known risk factors, like IVDU, tattooing, and service in Vietnam (14). Our finding of 10.1% is likely greater than the actual prevalence in our sample because of preferential testing of veterans with risk factors for HCV.

General recommendations for screening and testing have been established for those who have known risk factors for HCV, like a history of IVDU, tattoos, and blood transfusions before July 1992 (15, 16). The VA has also mandated screening and testing for HCV in the US veteran population that receives health care from the VA medical system (17). Very few studies have been conducted to guide HCV screening and testing policy in patients with chronic mental illness. Several cross-sectional studies in selected samples suggest that the prevalence of HCV among chronically mentally

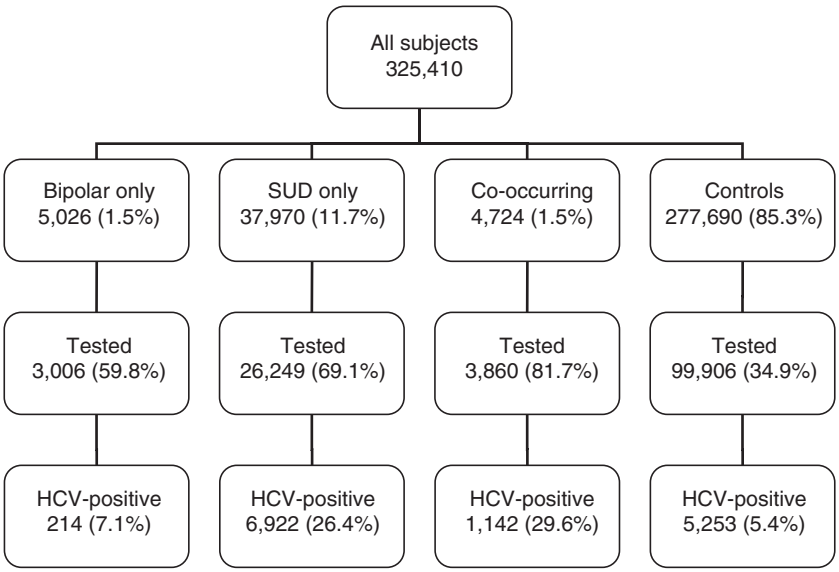

Fig. 1. Testing rates for the four subgroups. SUD = substance use disorder; HCV = hepatitis C.

ill patients may be 8–18% (18–21). One cross-sectional study of 4,310 bipolar veterans in the mid-Atlantic region examined for various medical comorbidities and found that 5.9% of subjects were HCV-positive (22). However, this study was not designed specifically to examine prevalence of HCV and did not differentiate bipolar patients with from those without a comorbid SUD.

A total of 3% of our sample were diagnosed with bipolar I, bipolar II or bipolar NOS, which, although high, is similar to the prevalence of these diagnoses in the general population (23, 24). Bipolar disorder may be overrepresented in veterans using Veterans Health Administration facilities as the VA Health Care Network is often a last resort, particularly for veterans without means or access to mental health care. Slightly less than 50% of our bipolar patients had a lifetime substance use comorbidity, which again is similar to findings in previously reported epidemiological studies (1, 2). In our study, 19.7% (1,356/6,866) of all tested veterans with BD (with or without a co-occurring SUD) were antibody-positive. This represented 13.8% (1,356/9,750) of all patients with BD who sought care, regardless of whether or not they had been tested. We found that 7.1% of patients in the BD group (without a history of SUD) and 29.6% of patients in the DD group who had been tested were positive for HCV. The DD group had a similar proportion of HCV-positive patients as the SUD group (29.6% versus 26.4%), suggesting that an SUD diagnosis increases the risk of HCV infection among bipolar veterans. Even patients in the bipolar group — those with no history of an SUD — were 1.3 times more likely than those in the control group to have HCV infection, which suggests that a diagnosis of BD may be a risk factor independent of SUD.

These findings suggest that BD and its associated behaviors confer an increased risk of HCV, even if BD patients do not have a comorbid SUD. This increased risk of HCV in bipolar patients may be due to undiagnosed current or past substance use, particularly IVDU. It may also be related to high-risk behaviors during manic episodes, including intermittent drug use or hypersexuality. Another hypothesis is related to BD's strong association with alcohol dependence (2). Alcohol dependence has been suspected of adversely affecting the immune response and thus may enhance transmission rates of HCV (25). Alcoholism may also contribute to other (non-IVDU) high-risk behaviors associated with contracting HCV (26).

Because alcohol dependence is relatively common in bipolar patients, HCV-positive bipolar patients may be at an overall greater risk for HCV-related hepatic morbidity and mortality. The lifetime prevalence of alcohol dependence in males diagnosed with BD is 49% and in females 29% (2). Testing and providing appropriate harm-reduction education or treating HCV in the bipolar population may reduce the progression of liver disease.

There are several limitations to the generalizability of our sample. The sample was older, mostly male, and composed solely of US veterans. Another limitation to our study is that it was of a retrospective database design and as such was subject to errors related to inaccuracies in medical record documentation. The design of this study did not allow us to explore whether all patients had

been screened for HCV and why patients had been tested for HCV, so the rates reflected in the tested sample may not represent the actual prevalence of HCV in this population. One of the strengths of this study is the large sample size and the fact that over 70% of all bipolar patients in our sample had been tested for HCV.

In conclusion, HCV is the most common blood-borne pathogen in the USA and has an even higher prevalence in veterans who use the services of Veterans Health Administration facilities than in the general population. Our study suggests that veterans with BD have a greater relative risk than controls of having HCV, even those without a history of substance abuse. Furthermore, the results of our study suggest that the prevalence of HCV is much higher in patients with BD than in the general population, at least in part because of comorbid substance use. Therefore, we would recommend that all patients with BD should be screened and tested for HCV, particularly if they have a comorbid SUD or other risk factors for HCV.

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